IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 10/649,457

Confirmation No. 5783

Applicant: Crystal et al.

Filed: August 27, 2003

TC/AU: 1632

Examiner: Marcia S. Noble

Docket No.: 216474 (Client Reference No. 3044-01 (US) BK)

Customer No.: 23460

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DECLARATION UNDER 37 C.F.R. § 1.132 OF RONALD G. CRYSTAL, M.D.

1. I, Ronald G. Crystal, M.D., am Chairman of Genetic Medicine at Weill Medical College of Cornell University and a co-inventor of the subject patent application.

2. The wild type nucleic acid sequence encoding *Bacillus anthracis* protective antigen (PA) contains 765 codons. Using codon optimization techniques, each of the 765 codons of the PA sequence could be modified, separately and in various combinations, to be codons that are expressed more frequently in humans than in *Bacillus anthracis*. As such, there are approximately 192 x 10^{373} of possible ways that the native PA sequence could be modified via codon-optimization.

3. Mogridge et al., *J. Bacteriol., 183*: 2111-2116 (2001), discloses mutations in domain 3 of the PA coding sequence generated via random mutagenesis, which mutations result in changes to the amino acid sequence of domain 3. In contrast, the modifications to the PA coding sequence of SEQ ID NO: 1 disclosed and claimed in the present application occur across the entire PA coding sequence and do not alter the PA amino acid sequence encoded thereby.

4. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 6-17-09

Ronald G. Crystal, M.D.